METHODS, APPARATUS AND SYSTEMS FOR CONCENTRATION, SEPARATION AND REMOVAL OF PARTICLES AT/FROM THE SURFACE OF DROPS

This application is a Divisional application of U.S. patent application Ser. No. 12/710,885, filed Feb. 23, 2010, which in turn claims the benefit under 35 U.S.C. §119(e) to U.S. Provisional Patent Application No. 61/208,319, filed Feb. 23, 2009, each of which is incorporated herein by reference in its entirety.

STATEMENT REGARDING FEDERALLY-SPONSORED RESEARCH AND DEVELOPMENT

This invention was made with government support under Grant Nos. 0626123 and 0626070 awarded by the National Science Foundation. The government has certain rights in this invention.

This invention relates to the field of digital microfluidics, the concentration and separation of particles on the surface of droplets and controlled coalescing of droplets.

An appealing approach to the issue of controlling fluids in microdevices is the use of droplets which can transport various types of fluids and particles. This has been referred to as "digital microfluidics." An advantage of this technique compared to those using fluid streams lies in its potential for programmable microchips with biochemical reactions occurring within single droplets. There are numerous other applications in which the presence of small particles on drop surfaces is important. First, it is well known that foams and emulsions can be stabilized by using submicron sized solid particles which become adsorbed at fluid-fluid interfaces, a technique often used in diverse applications. However, the physics behind the process by which stabilization occurs is still far from being understood. Second, in recent years, partly as a result of the attention given to nano particles (and nanotechnology), there has been much interest in the phenomenon of particles assembly at interfaces, including fluid-fluid interfaces, as a means to fabricate novel nano structured materials. Third, the field of digital microfluidics, which generates and uses droplets—rather than fluid streams—to transport, concentrate and mix fluid and particles, offers a clear advantage in its potential for programmable micro-chips with biochemical reactions occurring within single drops.

Concentration and binary separation of micro particles for droplet-based digital microfluids has already been accomplished by Cho, Zhao, and Kim (*Lab Chip* 2007, 7, 490-498). However, the present invention contains major advances over that process. The particles described in the Cho article were charged and underwent electrophoresis. Positively and negatively charged particles can thus be separated via that process. The methods described herein use particles that are not charged, so there is no charge related electric force acting on them. Instead, particles undergo dielectrophoresis, where the force is due to the gradient of the electric field. The method also has application for use with charged particles as dielectrophoresis itself acts on both charged and uncharged particles. At first sight, it is unexpected that the particles would undergo dielectrophoresis when a uniform external electric field is applied. However, the presence of the drop makes the electric field non-uniform in the vicinity and on the surface of the drop. Another major difference is that the particles described in the Cho article are within the droplets; while the particles in the present invention are at the drop's surface. Furthermore, the methods described herein can be used for separating two kinds of particles from a droplet as well as for washing the droplet. At the end of the process there are either one or two droplets completely free of particles. At the end of process described in the Cho article, there is no droplet without particles.

U.S. Pat. No. 7,267,752 discloses a method for rapid, size-based deposition of particles from liquid suspension using a non-uniform electric field. U.S. Pat. No. 5,814,200 discloses the use of non-uniform, alternating electric field which allows particles to undergo dielectrophoresis, thereby separating two different particles suspended in a medium. U.S. Pat. No. 4,305,797 separates particles within a mixture by passing the mixture through a non-uniform electric field generated between an electrically charged surface and a grounded surface. However, the methods described in those patents differ from those of the present disclosure in that they apply non-uniform electric fields while the methods described herein can use a uniform electric field. The methods disclosed in those patents are for particles suspended in a medium, while the methods described herein relates to particles on the surface of drops where they remain trapped because of the interfacial tension.

SUMMARY

Methods to concentrate or otherwise manipulate or move particles on the surface of a dispersed phase in a continuous phase are provided. Dispersed phases include liquid drops within a liquid or gas continuous phase or gaseous bubbles within a liquid continuous phase. As an example the dispersed phase is a liquid drop in an inmiscible continuous phase. The methods can be used to separate different types of particles on the drop or bubble either to remove them from the drop or bubble or to produce a pattern of particles on the drop or bubble, and to coalesce drops or bubbles. The technique uses an externally applied electric field that is typically uniform to move particles on a surface of a drop suspended in a medium. In an electric field, such as in a uniform field, the electric field's non-uniformity in the vicinity and on the surface of drop result in dielectrophoretic motion of the particles on the surface of the drop. Depending on the respective dielectric constants of the fluids and the particles, particles aggregate either near the poles or near the equator of the drop, creating a patterned structure (e.g., a Janus particle, which is optionally solidified). Also provided are solidified drops, optionally prepared according to the methods described herein, that comprise particles aggregated at their poles and/or equator. In one embodiment, the particles are uncharged.

In a Pickering emulsion, motion of stabilizing particles to either the poles or equator will leave "clear" portions that facilitate coalescence of the emulsion. This effect also can be used to mix two or more types of drops, for example, one comprising a substrate and another comprising an enzyme, to initiate an enzymatic reaction. Mixing may be enhanced in many instances if the drops have different sizes.

When particles aggregate near the poles and the dielectric constant of the drop or bubble is greater than that of the ambient fluid, the drop or bubble deformation is larger than that of a clean drop or bubble. In this case, with a further increase in the electric field, the drop or bubble develops conical ends and particles concentrated at the poles eject out by a tip streaming mechanism, thus leaving the drop or bubble free of particles. On the other hand, when particles aggregate near the equator, it is shown that the drop or bubble can be broken into three or more major droplets or bubbles, with the middle droplet or bubble carrying all particles and the two larger size droplets or bubbles on the sides being free of